Commercializing Successful Biomedical Technologies

Successful product design and development require the ability to take a concept and translate the technology into useful, patentable, commercial products.

For scientists and engineers, this book demystifies the commercialization process, guiding the reader through each practical stage, describing key issues including market analysis, product development, intellectual property and regulatory constraints.

- A robust product development plan is provided though a step-by-step model, from concept to regulated, commercially viable product.
- Key business issues are highlighted, taking into account critical business aspects, such as budgetary impact, time constraints, and quality control in the development cycle.
- Case studies and contributions from industry are included for a practical perspective.
- Learning points and exercises reinforce the most important concepts and strengthen understanding.

Written in a concise manner, this book will be the indispensable guide for professionals and entrepreneurs in biomedical technology development. With the increasing need for students to be fluent in such business skills, this book is an ideal accompaniment to a capstone design course in engineering and biotechnology.

Foreword written by **Frank L. Douglas Ph.D., M.D.** *Former Executive Vice President, member of Board of Management and Chief Scientific Officer of Aventis Pharmaceutical, Former Professor of the Practice and Executive Director of the MIT Center for Biomedical Innovation and Partner at Pure Tech Ventures.*

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Basic Principles for the Development of Drugs, Diagnostics and Devices

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To Gauri, whose continuing support and encouragement, whose patience and willingness to shoulder my share of parenting when necessary, and more, made the completion of this book possible. Without your help, there would have been no book.

Contents

Foreword

The deciphering of the human genome at the dawn of our twenty-first century not only fueled expectation of an increase in speed of developing therapies for many diseases but also exploded some cherished myths. Among the myths exploded was the belief that there were about 100 000 genes in the human genome and that this would lead to thousands of new 'targets' (receptors, enzymes, transporters, ion channels, etc.) for the discovery of new drugs. Although still somewhat in question, the number of genes in the human genome is felt to be about 30 000, thus dampening considerably some of the initial euphoria over the anticipated results of this outstanding achievement: the deciphering of the human genome. Another disappointing projection is that the number of druggable targets will only increase some threefold, from about 550 to 1500. Nonetheless, this incredible achievement, enabled by many technologies associated with genome sequencing, has fueled additional technologies, such as proteomics and metabolomics, for the innovation of new drugs and diagnostics.

The dawn of this century has also seen an increase in awareness of the importance of unwanted side effects in marketed drugs and safety issues in device usage. This debate has not only captured the attention of the public, as some widely used drugs, such as Vioxx and Pergolide, have been removed from the market, but also that of the Congress. Members of Congress have questioned whether there should be an agency separate from the Food and Drug Administration (FDA) to assess and monitor the safety of marketed drugs and devices.

In addition to the discussion of benefit and risk of new therapies, the cost of drugs is an increasingly popular topic of debate, along with the overall rapid rise of healthcare costs. The cost for major medical coverage has increased 124 percent above the consumer price index (CPI) every year since 1957. Meanwhile, the fully loaded cost of bringing a new drug to the market is over a billion dollars and only about one third of these drugs make more than $300 000 in sales per year.

Another challenge facing the industry, as the first decade of the twenty-first century ends, is the number of innovative drugs that will lose patent status and be converted to generics. Although this is good news for the consumer, it will be a challenge for the companies who innovated many of these drugs. For example, between 2004 and 2012, the top 15 pharmaceutical companies will see 95 of their drugs converted to generics. Thus in this first decade, these companies will lose billions of dollars in revenues.

It should be noted that manufacturing in devices and drugs has also had its challenges. Manufacturing problems at Chiron led to a potential shortage of flu vaccines in 2004 and manufacturing problems at Schering Plough led to significant loss of sales for their introduction of Clarinex. In fact, the FDA has had only modest success with their Process and Analytical Technology (PAT) initiative in their attempts to improve good manufacturing processes in the companies. Thirty-two serious Class 1 device recalls in the first six months of 2007 and 56 class I recalls in all of 2006 show that quality assurance and other manufacturing issues in the device industry continue. Thus, manufacturing remains an area for significant improvement and cost reduction in the industry.

Where then are the opportunities?

The first two decades of the twenty-first century will undoubtedly see the fulfillment of the hopes that genomic-based technologies, predictive modeling, automation, and miniaturization will revolutionize the way drugs are discovered, manufactured, and marketed. Two streams of importance will be the ability to identify that subset of patients that will best respond to a therapy and those patients who are likely to experience unwanted effects from that therapy. This will be the coming of age of "stratified medicine." Presently, Herceptin, for the treatement of a subset of breast cancers, is the best example. In this example, patients whose breast cancer is found to have HER2/neu receptors respond better to a regimen including Herceptin than to other regimens. Thus the diagnosis of the type of cancer and best therapy for that person are linked by a diagnostic. To be sure, not every therapy will lend itself to this unique constellation of diagnostic enabling therapy, as it is clear that at least three specific criteria will be necessary for this to occur. These criteria include the presence of: differential biological mechanisms, many treatment options, and a biological marker or diagnostic. The biological marker might be genomic-based, clinical observation, or imaging (M. R. Trusheim, E. R. Berndt, F. L. Douglas; Strategic and economic implications of stratified medicine, *Nature Reviews Drug Discovery*, April, 2007).

Another opportunity will be the combination of devices and therapy. A good example of this is the drug-eluting stent for the treatment of occluded coronary arteries. Other applications wait in areas such as diabetes, with the measurement of glucose accompanied by the release of the appropriate amount of insulin from an indwelling insulin reservoir. Other examples exist in cardiology and rheumatology, where measurement of arrhythmia or acute changes in an analyte by indwelling devices can lead to an appropriate release of drug to normalize the condition.

When stratified medicine becomes a standard part of the approach to healthcare, changes in the manner of commercialization will occur. It is quite likely that new commercialization paradigms that focus on specialists as opposed to the general practitioners will be associated with this approach. The supply chain issues will also be affected and perhaps there will be more opportunities for "just-in-time"

type approaches in the biopharmaceutical industry. The PAT initiative of the FDA may very well benefit this area.

A final area of progress will be in organizations and this is an arena where Dr Mehta's book will make a major contribution. Because of the complexity and the long times (8–15 years) involved with bringing a biomedical product (drugs, novel devices) from idea to market, few employees enter the industry with an appreciation of the pre-clinical, clinical, manufacturing, commercial and regulatory issues, and expertise needed to achieve this noble task of making novel medicines and devices accessible to patients. Dr Mehta's book not only introduces the reader to the nomenclature and issues but, through problem discussions, he gives the reader (student or industry employee) a sense of the complexity, the creativity as well as the regulatory requirements that must be satisfied to achieve the task. This book should improve the public's understanding of the challenge of innovating devices and drugs and thus improve the dialogue of benefit and risk decisions associated with the approval and marketing of devices and drugs.

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Preface

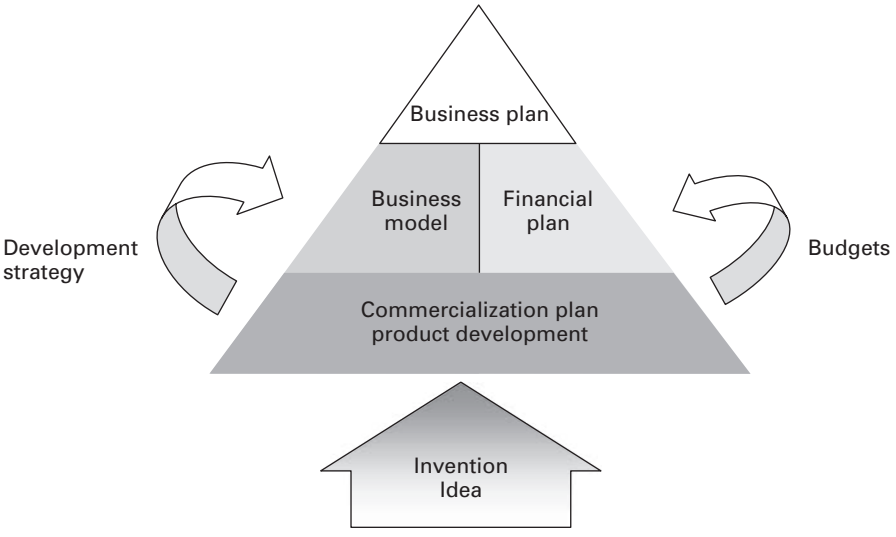
This book will help readers draw a roadmap of the process of taking a biomedical invention and creating a product that can pass regulatory approval to be successfully commercialized. The regulated products included in this context are drugs (both small molecules and biologics), medical devices, diagnostics, and their combination products, as defined by the Food and Drug Administration (FDA) – the regulatory agency that is responsible for overseeing the world's single largest healthcare market, the United States. The term "biomedical technologies" refers to the collective technologies underlying these FDA-regulated products: biotechnology, various engineering technologies, chemistry and materials science, etc.

The book highlights key issues that might help improve chances of success through the complete commercialization process for biomedical technologies and products. This text started as an expansion of a series of lectures given to students at the Lally School of Management and Technology, Rensselaer Polytechnic Institute in Troy, NY as part of a class called "Commercializing biomedical technology." However, going beyond the classroom in writing this book, information has been taken from many sources and experienced people from industry have contributed to add current and practical information to various segments of the book.

This book could be used to bring science and engineering students together with business and law students, and show them the benefits of approaching this complex process as a team. Many of these students have found the information useful in job interviews and in planning careers in the biotech industry and its service sectors.

This book has a practical perspective, so that current scientists, engineers and managers in the industry can apply these concepts, issues, and exercises within the context of their job functions in the industry. What's more, aspiring entrepreneurs may seek to apply these concepts to their invention or idea; walking through all the steps and exercises to create a sound commercialization plan that can form the basis for a business plan for a new venture (see figure).

Business models and financial plans vary with the economic or personal context and the goals of the founders. However, any business model, to be successful, must come from an understanding of the complete commercialization path for the regulated product. The linear roadmap shows the components that must be assessed to build a sound commercialization plan, but the processes are all carried out in parallel, with shifting emphasis on each component as one proceeds down the plan. The sequence of components is mirrored in the sequence of chapters in the



First you have to understand how your idea will be developed into a product and reach the paying customers; then you can choose one of many successful business models in the biomedical industry and prepare a business or financial plan to execute that development strategy.

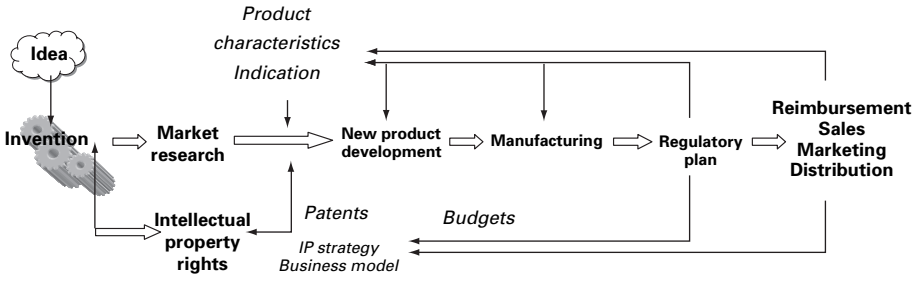
Components of a product commercialization plan and roadmap

Plan	Position	Patent	Product	Pass!	Production	Profits
Industry context	**Market research**	**Intellectual property rights**	**New product development (NPD)**	**Regulatory plan**	**Manufacture**	**Reimbursement**
Technology positioning and strategy, corporate portfolio strategy, industrial value chain context	Market need, Specific indication of interest, market size and segments, product characteristics	Intellectual property management and licensing strategy, Patent content for market protection, Business models	Stage gate new product testing and development plan, budget, Gannt chart	Regulatory strategy – working with FDA towards approval	Production planning	Coverage, Coding, Payment, Distribution, Marketing and sales planning

Roadmap to create a commercialization plan. The linear stages shown here reflect the layout of the book.

book. The arrows below the components in the roadmap illustrate the fact that all these components must be kept in mind to achieve a successful commercial and product development plan.

The process of doing science and also the process of building commercial entities can be represented as a linear thought process, but the practice of both is a



Successful development of new biomedical products for a competitive and regulated marketplace requires a full and thorough understanding of specific issues in the full value chain, discussed in the book. As feedback from various areas is defined for the specific product concept, the commercialization and product development plan will be revised (indicated by thinner feedback arrows above).

path-dependent, iterative process, where learning and understanding grow by doing each experiment or building each step of a commercialization plan. The schematic (above) illustrates, with arrows, the process of feedback between the various components of a commercialization process. As an example, the regulatory process influences the product development plan and also defines the markets accessed by the product. Likewise, access to intellectual property rights influences the direction of development and access to specific markets. Thus, iterative feedback from evaluating the specific regulatory pathways or intellectual property rights might require reconfiguration of the product characteristics or might require choosing a different application from that conceived during original invention.

The process for planning new product development might, for instance, follow the steps:

Idea – invention – market research – intellectual property search – define product and indications of interest – plan the key product development steps – check on regulatory strategy – revise product development plan and characteristics – check on reimbursement strategy – revise product characteristics and product development plan.

The result will be a comprehensive product development and commercialization plan with a timeline and budget. The exercises at the end of the chapters will help guide the reader through these steps.

While the original multidisciplinary (scientists, engineers, management, and other humanities students) course continues as a graduate-level course, much of the developed material has been incorporated into the Biomedical Engineering undergraduate capstone design course at Rensselaer Polytechnic Institute (RPI) as part of the core curriculum, hopefully creating a more conscious and self-aware breed of product development scientist and engineer.

Finally, it is my hope that better thinking and planning in the development of regulated products will help improve the efficiency, success, and quality of biomedical technology commercialization, increasing the number of innovative products that can be delivered to help people.

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The contributions and suggestions of friends and colleagues who shared their time, their insights from years of industry experience, their editorial suggestions, and specific case studies, have significantly improved this book. I would particularly like to recognize the formative early discussions and exchanges with my colleague Dr Jan Stegemann during the creation of the eponymous class that we co-taught at Rensselaer Polytechnic Institute (RPI).

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